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NEWS 5 SEP 29 DISSABS now available on STN
NEWS 6 OCT 10 PCTFULL: Two new display fields added
NEWS 7 OCT 21 BIOSIS file reloaded and enhanced
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=> s G-CSF
L1 17935 G-CSF

=> s l1 (5a) (polyethylene glycol)
L2 42 L1 (5A) (POLYETHYLENE GLYCOL)

=> d l2 1-42 bib ab

L2 ANSWER 1 OF 42 MEDLINE on STN
AN 97118551 MEDLINE
DN 97118551 PubMed ID: 8959393
TI Pharmacokinetics and pharmacodynamics of a recombinant human granulocyte colony-stimulating factor.
AU Kuwabara T; Kobayashi S; Sugiyama Y
CS Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, Japan.
SO DRUG METABOLISM REVIEWS, (1996 Nov) 28 (4) 625-58. Ref: 66
Journal code: 0322067. ISSN: 0360-2532.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970319
AB Granulocyte colony-stimulating factor (G-CSF), a hematopoietic growth factor, is a clinically effective drug used to promote neutrophil recovery in patients with chemo- or radiotherapy-induced neutropenia. We have reviewed the pharmacokinetic and pharmacodynamic properties of three kinds of G-CSFs: E. coli derived G-CSF, CHO-derived G-CSF, and mutein G-CSF. The clearances of G-CSFs are saturable and autoinducible in experimental animals and humans. That is, the systemic clearances of G-CSFs decrease as the dose injected increases and approaches a constant value. Both saturable and nonsaturable processes are involved in G-CSF elimination. Also, the systemic clearances of G-CSFs are increased by repeated administration of G-CSF. Although the relative bioavailability of G-CSFs after subcutaneous administration is approximately 60%, the increase in peripheral white blood cells or neutrophils is greater than that after intravenous administration at the same dose. The effects of G-CSFs seem to be time dependent rather than AUC dependent, considering that mean residence time of G-CSFs in the plasma is longer after subcutaneous administration than that after intravenous administration. There is a slight difference in the pharmacokinetics of E-coli- and CHO-G-CSF although they seem to be pharmacologically equivalent. The correlation

between G-CSF clearance and peripheral neutrophil counts in the patients suggests that G-CSF receptors contribute to G-CSF clearance. Quantitative pharmacokinetic analysis using mutein G-CSF shows that the G-CSF receptor plays a major role in saturable G-CSF clearance, and that this saturable process accounts for approximately 80% of the total clearance at low doses. That is, the degradation following the receptor-mediated endocytosis in bone marrow might be a major clearance system of G-CSF at a physiological blood level. The G-CSF receptor in bone marrow might work not only as a signal transducer for differentiation and proliferation of granulopoietic precursor cells but as a regulator of G-CSF levels in blood. In addition, at high doses, glomerular filtration in the kidneys is the major process for nonsaturable G-CSF clearance. At present, **polyethylene glycol** derivatives of **G-CSF** are being developed to reduce the frequency of G-CSF administration.

L2 ANSWER 2 OF 42 MEDLINE on STN
 AN 90338025 MEDLINE
 DN 90338025 PubMed ID: 1696260
 TI Purification and characterization of the receptor for murine granulocyte colony-stimulating factor.
 AU Fukunaga R; Ishizaka-Ikeda E; Nagata S
 CS Osaka Bioscience Institute, Japan.
 SO JOURNAL OF BIOLOGICAL CHEMISTRY, (1990 Aug 15) 265 (23) 14008-15.
 Journal code: 2985121R. ISSN: 0021-9258.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199009
 ED Entered STN: 19901012
 Last Updated on STN: 19970203
 Entered Medline: 19900913
 AB A receptor for mouse granulocyte colony-stimulating factor (G-CSF) has been found on the cell surface of mouse myeloid leukemia cell line NFS-60. Chemical cross-linking of the receptor with radioiodinated G-CSF, followed by gel electrophoresis in the presence of sodium dodecyl sulfate, has revealed that the G-CSF receptor in the NFS-60 cells is a single polypeptide of Mr approximately 100,000-130,000. The receptor in the membrane fraction of NFS-60 cells were solubilized in an active form with 3-[(3-cholamidopropyl) dimethylammonio]-1-propanesulfonic acid. The solubilized receptor was purified approximately 100,000-fold to near homogeneity using a G-CSF affinity gel and gel filtration on a Superose 12 column, as measured by the selective precipitation of the ¹²⁵I-G-CSF-receptor complex by **polyethylene glycol**. The purified G-CSF receptor has two classes of binding characteristics, one with an equilibrium dissociation constant (Kd) of 120-360 pM which is comparable with the Kd value for the cell-surface receptor, and the other with a higher Kd value of 2.6-4.2 nM. Analyses of the purified receptor by ligand blotting and sucrose density gradient centrifugation indicated that the low-affinity receptor is the monomer of the Mr 100,000-130,000 protein, whereas the high-affinity receptor consists of oligomers of the protein.

L2 ANSWER 3 OF 42 USPATFULL on STN
 AN 2004:24747 USPATFULL
 TI Method for refolding proteins containing free cysteine residues
 IN Rosendahl, Mary S., Broomfield, CO, UNITED STATES
 Cox, George N, Louisville, CO, UNITED STATES
 Doherty, Daniel H, Boulder, CO, UNITED STATES
 PI US 2004018586 A1 20040129
 AI US 2003-276358 A1 20030410 (10)
 WO 2001-US16088 20010516
 DT Utility

FS APPLICATION

LREP SHERIDAN ROSS PC, 1560 BROADWAY, SUITE 1200, DENVER, CO, 80202

CLMN Number of Claims: 55

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 5001

AB The present invention relates to novel methods for making and refolding insoluble or aggregated proteins having free cysteines in which a host cell expressing the protein is exposed to a cysteine blocking agent. The soluble, refolded proteins produced by the novel methods can then be modified to increase their effectiveness. Such modifications include attaching a PEG moiety to form PEGylated proteins.

L2 ANSWER 4 OF 42 USPATFULL on STN

AN 2003:311810 USPATFULL

TI Branched polyalkylene glycols

IN Yamasaki, Motoo, Tokyo, JAPAN

Suzawa, Toshiyuki, Tokyo, JAPAN

Murakami, Tatsuya, Tokyo, JAPAN

Sakurai, Noriko, Tokyo, JAPAN

Yamashita, Kinya, Shizuoka, JAPAN

Mukai, Mayumi, Shizuoka, JAPAN

Kuwabara, Takashi, Shizuoka, JAPAN

Ohta, So, Tokyo, JAPAN

Miki, Ichiro, Shizuoka, JAPAN

PI US 2003219404 A1 20031127

AI US 2002-168956 A1 20020624 (10)

WO 2000-JP9159 20001222

PRAI JP 1999-366312 19991224

DT Utility

FS APPLICATION

LREP FITZPATRICK CELLA HARPER & SCINTO, 30 ROCKEFELLER PLAZA, NEW YORK, NY, 10112

CLMN Number of Claims: 16

ECL Exemplary Claim: 1

DRWN 2 Drawing Page(s)

LN.CNT 3707

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides branched polyalkylene glycols useful as a chemically modifying agent for physiologically active polypeptides, wherein two single-chain polyalkylene glycols are linked to a group having a cyclic structure other than a plane structure, and wherein a group having reactivity with an amino acid side chain, an N-terminal amino group or a C-terminal carboxyl group in a polypeptide or a group convertible into the group having reactivity is linked to the group having a structure other than a plane structure.

L2 ANSWER 5 OF 42 USPATFULL on STN

AN 2003:295028 USPATFULL

TI Pseudo native chemical ligation

IN Hunter, Christie L., San Mateo, CA, UNITED STATES

Botti, Paolo, Piacenza, ITALY

Bradburne, James A., Redwood City, CA, UNITED STATES

Chen, Shiah-yun, Mountain View, CA, UNITED STATES

Cressman, Sonya, Ladysmith, CANADA

Kent, Stephen B.H., San Francisco, CA, UNITED STATES

Kochendoerfer, Gerd G., Oakland, CA, UNITED STATES

Low, Donald W., Burlingame, CA, UNITED STATES

PI US 2003208046 A1 20031106

AI US 2003-332386 A1 20030108 (10)

WO 2001-US21935 20010712

DT Utility

FS APPLICATION

LREP LINIAK, BERENATO & WHITE, LLC, 6550 ROCK SPRING DRIVE, SUITE 240,

BETHESDA, MD, 20817
CLMN Number of Claims: 62
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 3123

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention concerns methods and compositions for extending the technique of native chemical ligation of a wider range of peptides, polypeptides, other polymers and other molecules via an amide bond (see FIG. 1). The invention further provides methods and uses for such proteins and derivatized proteins. The invention is particularly suitable for use in the synthesis of optionally polymer-modified, synthetic bioactive proteins, and of pharmaceutical compositions that contain such proteins. ##STR1##

L2 ANSWER 6 OF 42 USPATFULL on STN

AN 2003:289296 USPATFULL

TI Chemically modified G-CSF

IN Ishikawa, Rika, Tokyo, JAPAN

Okada, Yuji, Gunma-ken, JAPAN

Kakitani, Makoto, Gunma-ken, JAPAN

PA KIRIN-AMGEN (non-U.S. corporation)

PI US 2003204057 A1 20031030

AI US 2003-436784 A1 20030512 (10)

RLI Division of Ser. No. US 2001-921114, filed on 2 Aug 2001, PENDING

Continuation of Ser. No. US 2000-518896, filed on 6 Mar 2000, ABANDONED

~~Continuation of Ser. No. US 1997-957719, filed on 27 Oct 1997, GRANTED,~~

~~Pat. No. US 6166183 Continuation of Ser. No. US 1992-983620, filed on 30~~

~~Nov. 1992, GRANTED, Pat. No. US 5824778 Continuation of Ser. No. US~~

~~1990-566451, filed on 1 Oct 1990, ABANDONED~~

PRAI JP 1988-324747 19881222

JP 1989-199176 19890731

DT Utility

FS APPLICATION

LREP MARSHALL, GERSTEIN & BORUN LLP, 6300 SEARS TOWER, 233 S. WACKER DRIVE,
CHICAGO, IL, 60606

CLMN Number of Claims: 3

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 658

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a chemically-modified protein prepared by binding polyethylene glycol to a polypeptide characterized by being the product of expression by a host cell of an exogenous DNA sequence and substantially having the following amino acid sequence:

(Het) n

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu
Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys
Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu
Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu Ala
Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln
Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu
Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Het Glu Glu Leu Gly Het
Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Het Pro Ala Phe Ala Ser Ala Phe
Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu
Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro

(n=0 or 1)

The chemically-modified protein according to the present invention has a neutrophils-increasing activity much more lasted than that of the intact human G-CSF, enabling fewer numbers of administration with a lower dose.

L2 ANSWER 7 OF 42 USPATFULL on STN
 AN 2003:264781 USPATFULL
 TI Oral delivery of chemically modified proteins
 IN Habberfield, Alan D., Pacific Palisades, CA, UNITED STATES
 PA Amgen Inc. (U.S. corporation)
 PI US 2003185795 A1 20031002
 AI US 2003-345639 A1 20030115 (10)
 RLI Continuation of Ser. No. US 2001-818430, filed on 26 Mar 2001, ABANDONED
 Continuation of Ser. No. US 1997-910814, filed on 13 Aug 1997, ABANDONED
 Continuation of Ser. No. US 1996-753901, filed on 3 Dec 1996, ABANDONED
 Continuation of Ser. No. US 1995-379121, filed on 1 Feb 1995, ABANDONED
 Continuation-in-part of Ser. No. US 1994-361016, filed on 21 Dec 1994,
 ABANDONED Continuation of Ser. No. US 1994-194187, filed on 8 Feb 1994,
 ABANDONED
 DT Utility
 FS APPLICATION
 LREP AMGEN INCORPORATED, MAIL STOP 27-4-A, ONE AMGEN CENTER DRIVE, THOUSAND
 OAKS, CA, 91320-1799
 CLMN Number of Claims: 12
 ECL Exemplary Claim: 1
 DRWN 16 Drawing Page(s)
 LN.CNT 1855
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB Provided are compositions and methods for oral delivery of chemically
 modified proteins, including chemically modified G-CSF and chemically
 modified consensus interferon. Uptake from the intestine to the
 bloodstream is demonstrated for pegylated G-CSF and pegylated consensus
 interferon.

L2 ANSWER 8 OF 42 USPATFULL on STN
 AN 2003:201595 USPATFULL
 TI Composition containing biologically active polypeptides suitable for the
 oral administration
 IN Wang, Kai Hua, San Bruno, CA, UNITED STATES
 PI US 2003139582 A1 20030724
 AI US 2002-50017 A1 20020117 (10)
 DT Utility
 FS APPLICATION
 LREP John H. Faro, Esq., Faro & Associates, P.A., P.O. Box 4904, Key
 Biscayne, FL, 33149-4904
 CLMN Number of Claims: 10
 ECL Exemplary Claim: 1
 DRWN No Drawings
 LN.CNT 494
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 AB A hydrophilic emulsion composition as a carrier fluid for the oral
 administration of biologically active polypeptides. The composition
 consists of a commercial therapeutic polypeptide product, e.g.,
 Granulocyte Colony Stimulating Factor (G-CSF), and a carrier fluid
 containing a small molecule spleen extract and a fluid mixture of
 substances that are complimentary to said small molecule extract to
 protect the polypeptide and promote the absorption of the polypeptide by
 epithelium of intestinal mucosa.

L2 ANSWER 9 OF 42 USPATFULL on STN
 AN 2003:140559 USPATFULL
 TI N-terminally chemically modified protein compositions and methods
 IN Kinstler, Olaf B., Thousand Oaks, CA, UNITED STATES
 PA Amgen, Inc. (U.S. corporation)
 PI US 2003096400 A1 20030522
 AI US 2002-264846 A1 20021004 (10)
 RLI Continuation of Ser. No. US 2002-131956, filed on 25 Apr 2002, PENDING
 Continuation of Ser. No. US 2001-817725, filed on 26 Mar 2001, PENDING

Continuation of Ser. No. US 1999-408113, filed on 29 Sep 1999, ABANDONED
Division of Ser. No. US 1997-879760, filed on 20 Jun 1997, GRANTED, Pat.
No. US 5985265 Continuation of Ser. No. US 1994-321510, filed on 12 Oct
1994, GRANTED, Pat. No. US 5824784

DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO,
IL, 60606-6357
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 1409

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided herein are methods and compositions relating to the attachment
of water soluble polymers to proteins. Provided are novel methods for
N-terminally modifying proteins or analogs thereof, and resultant
compositions, including novel chemically modified G-CSF compositions and
related methods of preparation.

L2 ANSWER 10 OF 42 USPATFULL on STN
AN 2003:136792 USPATFULL
TI Pulmonary administration of granulocyte colony stimulating factor
IN Niven, Ralph, Camarillo, CA, United States
Pitt, Colin G, Thousand Oaks, CA, United States
PA Amgen, Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 6565841 B1 20030520
AI US 1993-28087 19930308 (8)
RLI Continuation-in-part of Ser. No. US 1992-953208, filed on 29 Sep 1992,
now patented, Pat. No. US 5284656 Continuation of Ser. No. US
1991-669792, filed on 15 Mar 1991, now abandoned

DT Utility
FS GRANTED
EXNAM Primary Examiner: Achutamurthy, Ponnathapu; Assistant Examiner: Kerr,
Kathleen
LREP Crandall, Craig A., Levy, Ron K., Odre, Steven M.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1282

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions for pulmonary delivery of chemically modified
G-CSF, and pegylated proteins are disclosed.

L2 ANSWER 11 OF 42 USPATFULL on STN
AN 2003:120198 USPATFULL
TI Fc fusion proteins of human granulocyte colony-stimulating factor with
increased biological activities
IN Sun, Lee-Hwei K., Houston, TX, UNITED STATES
Sun, Bill N. C., Bellaire, TX, UNITED STATES
Sun, Cecily R. Y., Bellaire, TX, UNITED STATES
PI US 2003082679 A1 20030501
AI US 2001-968362 A1 20011001 (9)

DT Utility
FS APPLICATION
LREP Mr. Hsiang-ning Sun, 4212 Villanova Street, Houston, TX, 77005
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN 7 Drawing Page(s)
LN.CNT 740

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fc fusion proteins of human G-CSF with increased biological activities
relative to rhG-CSF on a molar basis are disclosed. The hG-CSF-L-vFc
fusion protein comprises hG-CSF, a flexible peptide linker of about 20
or fewer amino acids, and a human IgG Fc variant. The Fc variant is of a

non-lytic nature and shows minimal undesirable Fc-mediated side effects. A method is also disclosed to make or produce such fusion proteins at high expression levels. Such hG-CSF-L-vFc fusion proteins exhibit extended serum half-life and increased biological activities, leading to improved pharmacokinetics and pharmacodynamics, thus fewer injections will be needed within a period of time.

L2 ANSWER 12 OF 42 USPATFULL on STN
AN 2003:78062 USPATFULL
TI N-terminally chemically modified protein compositions and methods
IN Kinstler, Olaf B., Thousand Oaks, CA, UNITED STATES
PI US 2003053982 A1 20030320
AI US 2002-131956 A1 20020425 (10)
RLI Continuation of Ser. No. US 2001-817725, filed on 26 Mar 2001, PENDING
Continuation of Ser. No. US 1999-408113, filed on 29 Sep 1999, ABANDONED
Division of Ser. No. US 1997-879760, filed on 20 Jun 1997, GRANTED, Pat.
No. US 5985265 Continuation of Ser. No. US 1994-312510, filed on 26 Sep
1994, GRANTED, Pat. No. US 5802704
DT Utility
FS APPLICATION
LREP MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO,
IL, 60606-6357
CLMN Number of Claims: 38
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 1396
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided herein are methods and compositions relating to the attachment
of water soluble polymers to proteins. Provided are novel methods for
N-terminally modifying proteins or analogs thereof, and resultant
compositions, including novel chemically modified G-CSF compositions and
related methods of preparation.

L2 ANSWER 13 OF 42 USPATFULL on STN
AN 2002:315200 USPATFULL
TI Chemically-modified G-CSF
IN Ishikawa, Rika, Tokyo, JAPAN
Okada, Yuji, Maebashi-shi, JAPAN
Kakitani, Makoto, Maebashi-shi, JAPAN
PA Kirin-Amgen, Inc., (non-U.S. corporation)
PI US 2002177688 A1 20021128
AI US 2001-921114 A1 20010802 (9)
RLI Continuation of Ser. No. US 2000-518896, filed on 6 Mar 2000, ABANDONED
Continuation of Ser. No. US 1997-957719, filed on 27 Oct 1997, PATENTED
Continuation of Ser. No. US 1992-983620, filed on 30 Nov 1992, PATENTED
Continuation of Ser. No. US 1990-566451, filed on 1 Oct 1990, ABANDONED
PRAI JP 1988-324747 19881222
JP 1989-199176 19890731
DT Utility
FS APPLICATION
LREP MARSHALL, O'TOOLE, GERSTEIN, MURRAY & BORUN, 6300 SEARS TOWER, 233 SOUTH
WACKER DRIVE, CHICAGO, IL, 60606-6402
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 5 Drawing Page(s)
LN.CNT 602
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a chemically-modified protein prepared by
binding polyethylene glycol to a polypeptide characterized by being the
product of expression by a host cell of an exogenous DNA sequence and
substantially having the following amino acid sequence:

(Met) n

Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln
 Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg
 Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu
 Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro
 Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly
 Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser
 Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln
 Leu His Ser Gly Leu Phe Leu Tyr Gln Gly Leu
 Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu
 Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
 Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Het
 Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro
 Thr Gln Gly Ala Het Pro Ala Phe Ala Ser Ala
 Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala
 Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr
 Arg Val Leu Arg His Leu Ala Gln Pro

(n = 0 or 1)

The chemically-modified protein according to the present invention has a
 neutrophils-increasing activity much more lasted than that of the intact
 human G-CSF, enabling fewer numbers of administration with a lower dose.

L2 ANSWER 14 OF 42 USPTAFULL on STN
 AN 2002:273360 USPTAFULL
 TI G-CSF analog compositions and methods
 IN Sarkar, Casim A., Cambridge, MA, UNITED STATES
 Lauffenburger, Douglas A., Cambridge, MA, UNITED STATES
 PI US 2002151488 A1 20021017
 AI US 2001-950473 A1 20010910 (9)
 PRAI US 2000-231464P 20000908 (60)
 DT Utility
 FS APPLICATION
 LREP MARSHALL, GERSTEIN & BORUN, 6300 SEARS TOWER, 233 SOUTH WACKER, CHICAGO,
 IL, 60606-6357
 CLMN Number of Claims: 19
 ECL Exemplary Claim: 1
 DRWN 1 Drawing Page(s)
 LN.CNT 2335

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to granulocyte colony stimulating factor
 ("G-CSF") polypeptide analog compositions. The concept detailed herein
 provides methods for screening G-CSF analogs, designed with one or more
 substitutions to amino acids, and selecting analogs for use as G-CSF
 replacements or antagonists, and may be generalizable beyond G-CSF
 analogs as well. In addition, pharmaceutical compositions and methods of
 use are provided for analogs so selected.

L2 ANSWER 15 OF 42 USPATFULL on STN
AN 2002:186080 USPATFULL
TI Oral delivery of chemically modified proteins
IN Habberfield, Alan D., Pacific Palisades, CA, UNITED STATES
PA Amgen Inc. (U.S. corporation)
PI US 2002099001 A1 20020725
AI US 2001-818430 A1 20010326 (9)
RLI Continuation of Ser. No. US 1997-910814, filed on 13 Aug 1997, ABANDONED
Continuation of Ser. No. US 1996-753901, filed on 3 Dec 1996, ABANDONED
Continuation of Ser. No. US 1995-379121, filed on 1 Feb 1995, ABANDONED
Continuation-in-part of Ser. No. US 1994-361016, filed on 21 Dec 1994,
ABANDONED Continuation of Ser. No. US 1994-194187, filed on 8 Feb 1994,
ABANDONED
DT Utility
FS APPLICATION
LREP U. S. Patent Operations/CAC, Dept. 4300, M/S 27-4-A, AMGEN, INC, One
Amgen Center Drive, Thousand Oaks, CA, 91320-1799
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 16 Drawing Page(s)
LN.CNT 1851
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are compositions and methods for oral delivery of chemically
modified proteins, including chemically modified G-CSF and chemically
modified consensus interferon. Uptake from the intestine to the
bloodstream is demonstrated for pegylated G-CSF and pegylated consensus
interferon.

L2 ANSWER 16 OF 42 USPATFULL on STN
AN 2001:190931 USPATFULL
TI Modulators of body weight, corresponding nucleic acids and proteins, and
diagnostic and therapeutic uses thereof
IN Friedman, Jeffrey M., New York, NY, United States
Zhang, Yiyang, New York, NY, United States
Proenca, Ricardo, Astoria, NY, United States
PA The Rockefeller University, NY, NY, United States (U.S. corporation)
PI US 6309853 B1 20011030
AI US 1995-483211 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1995-438431, filed on 10 May 1995
Continuation-in-part of Ser. No. US 1994-347563, filed on 30 Nov 1994,
now patented, Pat. No. US 5936810 Continuation-in-part of Ser. No. US
1994-292345, filed on 17 Aug 1994, now patented, Pat. No. US 6001968
DT Utility
FS GRANTED
EXNAM Primary Examiner: Yucel, Remy
LREP Klauber & Jackson
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 61 Drawing Page(s)
LN.CNT 6074
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates generally to the control of body weight of
animals including mammals and humans, and more particularly to materials
identified herein as modulators of body weight, and to diagnostic and
therapeutic uses of such modulators. In its broadest aspect, the present
invention relates to nucleotide sequences corresponding to the murine
and human OB gene, and two isoforms thereof, and proteins expressed by
such nucleotides or degenerate variations thereof, that demonstrate the
ability to participate in the control of mammalian body weight and that
have been postulated to play a critical role in the regulation of body
weight and adiposity. The present invention further provides nucleic
acid molecules for use as molecular probes or as primers for polymerase
chain reaction (PCR) amplification. In further aspects, the present
invention provides cloning vectors and mammalian expression vectors

comprising the nucleic acid molecules of the invention. The invention further relates to host cells transfected or transformed with an appropriate expression vector and to their use in the preparation of the modulators of the invention. Also provided are antibodies to the OB polypeptide. Moreover, a method for modulating body weight of a mammal is provided.

L2 ANSWER 17 OF 42 USPATFULL on STN
AN 2001:86442 USPATFULL
TI Polyol:oil suspensions for the sustained release of proteins
IN Goldenberg, Merrill, Thousand Oaks, CA, United States
Shan, Daxian, Thousand Oaks, CA, United States
Beekman, Alice, Thousand Oaks, CA, United States
PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 6245740 B1 20010612
AI US 1998-221181 19981223 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Moezie, F. T.
LREP Crandall, Craig A., Levy, Ron K., Odre, Steven M.
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 716

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to the preparation of polyol/thickened oil suspensions containing a biologically active agent, for the sustained delivery of the biologically active agent. The described protein/glycerol/oil suspensions show sustained release of protein, e.g., G-CSF, of up to at least one week.

L2 ANSWER 18 OF 42 USPATFULL on STN
AN 2000:174809 USPATFULL
TI Chemically-modified G-CSF
IN Ishikawa, Rika, Higashiyamato, Japan
Okada, Yuji, Maebashi, Japan
Kakitani, Makoto, Maebashi, Japan
PA Kirin-Amgen, Inc., Tokyo, Japan (non-U.S. corporation)
PI US 6166183 20001226
AI US 1997-957719 19971027 (8)
RLI Continuation of Ser. No. US 1992-983620, filed on 30 Nov 1992, now patented, Pat. No. US 5824778, issued on 20 Oct 1998 which is a continuation of Ser. No. US 566451
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Marshall, O'Toole, Gerstein, Murray & Borun
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 611

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a chemically-modified protein prepared by binding polyethylene glycol to a polypeptide characterized by being the product of expression by a host cell of an exogenous DNA sequence and substantially having the following amino acid sequence:
(Het)n - Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln - Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg - Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu - Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro - Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly - Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser - Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln - Leu His Ser Gly Leu Phe Leu Tyr Gln GIY Leu - Leu Gln Ala Leu Gly Ile Ser Pro Gln Leu - Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val - Ala Asp Phe Ala Thr Tbr Ile Trp Gln Gln Het - Glu Glu Leu Gly Het Ala Pro Ala Leu Gln

Pro - Thr Gln Gly Ala Het Pro Ala Phe Ala Ser Ala - Phe Gln Arg Arg
 Ala Gly Gly Val Leu Val Ala - Ser His Leu Gln Ser Phe Leu Glu Val Scr
 Tyr - Arg Val Leu Arg His Leu Ala Gln Pro (n = 0 or 1)

The chemically-modified protein according to the present invention has a neutrophils-increasing activity much more lasted than that of the intact human G-CSF, enabling fewer numbers of administration with a lower dose.

L2 ANSWER 19 OF 42 USPATFULL on STN
 AN 2000:128480 USPATFULL
 TI Nucleic acid primers and probes for the mammalian OB gene
 IN Friedman, Jeffrey M., New York, NY, United States
 Zhang, Yiying, New York, NY, United States
 Proenca, Ricardo, Astoria, NY, United States
 Maffei, Margherita, New York, NY, United States
 PA The Rockefeller University, NY, United States (U.S. corporation)
 PI US 6124448 20000926
 AI US 1995-488208 19950607 (8)
 RLI Continuation-in-part of Ser. No. US 1995-438431, filed on 10 May 1995
 which is a continuation-in-part of Ser. No. US 1994-347563, filed on 30
 Nov 1994, now patented, Pat. No. US 5935810 which is a
 continuation-in-part of Ser. No. US 1994-292345, filed on 17 Aug 1994
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Railey, II, Johnny F.
 LREP Klauber & Jackson
 CLMN Number of Claims: 4
 ECL Exemplary Claim: 1
 DRWN 61 Drawing Figure(s); 61 Drawing Page(s)
 LN.CNT 7089

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the control of body weight of animals including mammals and humans, and more particularly to materials identified herein as modulators of weight, and to the diagnostic and therapeutic uses to which such modulators may be put. In its broadest aspect, the present invention relates to the elucidation and discovery of nucleotide sequences, and proteins putatively expressed by such nucleotides or degenerate variations thereof, that demonstrate the ability to participate in the control of mammalian body weight. The nucleotide sequences in object represent the genes corresponding to the murine and human ob gene, that have been postulated to play a critical role in the regulation of body weight and adiposity. Preliminary data, presented herein, suggests that the polypeptide product of the gene in question functions as a hormone. The present invention further provides nucleic acid molecules for use as molecular probes, or as primers for polymerase chain reaction (PCR) amplification, i.e., synthetic or natural oligonucleotides. In further aspects, the present invention provides a cloning vector, which comprises the nucleic acids of the invention; and a bacterial, insect, or a mammalian expression vector, which comprises the nucleic acid molecules of the invention, operatively associated with an expression control sequence. Accordingly, the invention further relates to a bacterial or a mammalian cell transfected or transformed with an appropriate expression vector, and correspondingly, to the use of the above mentioned constructs in the preparation of the modulators of the invention. Also provided are antibodies to the ob polypeptide. Moreover, a method for modulating body weight of a mammal is provided. In specific examples, genes encoding two isoforms of both the murine and human ob polypeptides are provided.

L2 ANSWER 20 OF 42 USPATFULL on STN
 AN 2000:128471 USPATFULL
 TI OB polypeptide antibodies and method of making
 IN Friedman, Jeffrey M., New York, NY, United States
 Zhang, Yiying, New York, NY, United States

Proenca, Ricardo, Astoria, NY, United States
PA The Rockefeller University, New York, NY, United States (U.S. corporation)
PI US 6124439 20000926
AI US 1995-488214 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1995-438431, filed on 10 May 1995 which is a continuation-in-part of Ser. No. US 1994-347563, filed on 30 Nov 1994 which is a continuation-in-part of Ser. No. US 1994-292345, filed on 17 Aug 1994
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Klauber & Jackson
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN 68 Drawing Figure(s); 61 Drawing Page(s)
LN.CNT 6777

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the control of body weight of animals including mammals and humans, and more particularly to materials identified herein as modulators of body weight, and to diagnostic and therapeutic uses of such modulators. In its broadest aspect, the present invention relates to nucleotide sequences corresponding to the murine and human OB gene, and two isoforms thereof, and proteins expressed by such nucleotides or degenerate variations thereof, that demonstrate the ability to participate in the control of mammalian body weight and that have been postulated to play a critical role in the regulation of body weight and adiposity. The present invention further provides nucleic acid molecules for use as molecular probes or as primers for polymerase chain reaction (PCR) amplification. In further aspects, the present invention provides cloning vectors and mammalian expression vectors comprising the nucleic acid molecules of the invention. The invention further relates to host cells transfected or transformed with an appropriate expression vector and to their use in the preparation of the modulators of the invention. Also provided are antibodies to the OB polypeptide. Moreover, a method for modulating body weight of a mammal is provided.

L2 ANSWER 21 OF 42 USPATFULL on STN
AN 2000:44077 USPATFULL
TI OB polypeptides as modulators of body weight
IN Friedman, Jeffrey M., New York, NY, United States
Zhang, Yiyang, New York, NY, United States
Proenca, Ricardo, Astoria, NY, United States
PA The Rockefeller University, United States (U.S. corporation)
PI US 6048837 20000411
AI US 1995-485942 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1995-438431, filed on 10 May 1995 which is a continuation-in-part of Ser. No. US 1994-347563, filed on 30 Nov 1994 which is a continuation-in-part of Ser. No. US 1994-292345, filed on 17 Aug 1994
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Klauber & Jackson
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 61 Drawing Page(s)
LN.CNT 7390

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates generally to the control of body weight of animals including mammals and humans, and more particularly to materials identified herein as modulators of body weight, and to diagnostic and therapeutic uses of such modulators. In its broadest aspect, the present

invention relates to nucleotide sequences corresponding to the murine and human OB gene, and two isoforms thereof, and proteins expressed by such nucleotides or degenerate variations thereof, that demonstrate the ability to participate in the control of mammalian body weight and that have been postulated to play a critical role in the regulation of body weight and adiposity. The present invention further provides nucleic acid molecules for use as molecular probes or as primers for polymerase chain reaction (PCR) amplification. In further aspects, the present invention provides cloning vectors and mammalian expression vectors comprising the nucleic acid molecules of the invention. The invention further relates to host cells transfected or transformed with an appropriate expression vector and to their use in the preparation of the modulators of the invention. Also provided are antibodies to the OB polypeptide. Moreover, a method for modulating body weight of a mammal is provided.

L2 ANSWER 22 OF 42 USPATFULL on STN
AN 1999:145965 USPATFULL
TI N-terminally chemically modified protein compositions and methods
IN Kinstler, Olaf B., Thousand Oaks, CA, United States
Gabriel, Nancy E., Newbury Park, CA, United States
Farrar, Christine E., Newbury Park, CA, United States
DePrince, Randolph B., Raleigh, NC, United States
PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 5985265 19991116
AI US 1997-879760 19970620 (8)
RLI Continuation of Ser. No. US 1994-321510, filed on 12 Oct 1994, now patented, Pat. No. US 5824784
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura
LREP Crandall, Craig A., Levy, Ron K., Odre, Steven M.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1,2
DRWN 15 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 1278
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided herein are methods and compositions relating to the attachment of water soluble polymers to proteins. Provided are novel methods for N-terminally modifying proteins or analogs thereof, and resultant compositions, including novel chemically modified G-CSF compositions and related methods of preparation. Also provided is chemically modified consensus interferon.

L2 ANSWER 23 OF 42 USPATFULL on STN
AN 1999:24301 USPATFULL
TI Stable protein: phospholipid compositions and methods
IN Collins, David, Thousand Oaks, CA, United States
Cha, Younsik, Salt Lake City, UT, United States
Brems, David, Newbury Park, CA, United States
PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 5874075 19990223
AI US 1995-414161 19950331 (8)
RLI Continuation-in-part of Ser. No. US 1994-361011, filed on 21 Dec 1994, now abandoned which is a continuation of Ser. No. US 1993-132413, filed on 6 Oct 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John; Assistant Examiner: Saoud, Christine
LREP Crandall, Craig A., Levy, Ron K., Odre, Steven M.
CLMN Number of Claims: 42
ECL Exemplary Claim: 1
DRWN 35 Drawing Figure(s); 35 Drawing Page(s)
LN.CNT 1487

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to stable compositions of proteins and related methods wherein a protein capable of transitioning into the molten globular state is contacted with a negatively charged lipid vesicle, thereby stabilizing the protein against thermally-induced aggregation, denaturation, and loss of activity. The protein:phospholipid complex directly stabilizes the secondary and tertiary structure of the protein, and the compositions are useful in high temperature formulations and in novel delivery vehicles.

L2 ANSWER 24 OF 42 USPATFULL on STN

AN 1998:128368 USPATFULL

TI N-terminally chemically modified protein compositions and methods

IN Kinstler, Olaf B., Thousand Oaks, CA, United States

Gabriel, Nancy E., Newbury Park, CA, United States

Farrar, Christine E., Newbury Park, CA, United States

DePrince, Randolph B., Raleigh, NC, United States

PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)

PI US 5824784 19981020

AI US 1994-321510 19941012 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Achutamurthy, Ponnathapura

LREP Winter, Robert B., Pessin, Karol M., Odre, Steven M.

CLMN Number of Claims: 12

ECL Exemplary Claim: 1

DRWN 15 Drawing Figure(s); 15 Drawing Page(s)

LN.CNT 1289

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided herein are methods and compositions relating to the attachment of water soluble polymers to proteins. Provided are novel methods for N-terminally modifying proteins or analogs thereof, and resultant compositions, including novel N-terminally chemically modified G-CSF compositions and related methods of preparation. Also provided is chemically modified consensus interferon.

L2 ANSWER 25 OF 42 USPATFULL on STN

AN 1998:128363 USPATFULL

TI Chemically-modified G-CSF

IN Ishikawa, Rika, Higashiyamato, Japan

Okada, Yuji, Maebashi, Japan

Kakitani, Makoto, Maebashi, Japan

PA Kirin-Amgen, Inc., Thousand Oaks, CA, United States (U.S. corporation)

PI US 5824778 19981020

AI US 1992-983620 19921130 (7)

RLI Continuation of Ser. No. US 1989-566451, filed on 22 Dec 1989, now abandoned

PRAI JP 1988-324747 19881222

JP 1989-199176 19890731

DT Utility

FS Granted

EXNAM Primary Examiner: Ulm, John

LREP Marshall, O'Toole, Gerstein, Murray & Borun

CLMN Number of Claims: 2

ECL Exemplary Claim: 1

DRWN 5 Drawing Figure(s); 5 Drawing Page(s)

LN.CNT 569

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides a chemically-modified protein prepared by binding polyethylene glycol to a polypeptide characterized by being the product of expression by a host cell of an exogenous DNA sequence and substantially having the following amino acid sequence: ##STR1## The chemically-modified protein according to the present invention has a much longer lasting neutrophil-increasing activity than that of the

intact human G-CSF, enabling fewer numbers of administration with a lower dose.

L2 ANSWER 26 OF 42 USPATFULL on STN
AN 1998:75726 USPATFULL
TI Conjugate of a solution stable G-CSF derivative and a water-soluble polymer
IN Camble, Roger, Macclesfield, England
Timms, David, Macclesfield, England
Wilkinson, Anthony James, Macclesfield, England
PA Zeneca Limited, London, United Kingdom (non-U.S. corporation)
PI US 5773581 19980630
AI US 1995-488457 19950607 (8)
RLI Continuation of Ser. No. US 1993-155327, filed on 22 Nov 1993, now abandoned which is a division of Ser. No. US 1991-734225, filed on 22 Jul 1991, now patented, Pat. No. US 5320840
PRAI GB 1990-16138 19900723
GB 1990-18414 19900823
GB 1990-18415 19900823
GB 1990-18416 19900823
GB 1990-18417 19900823
GB 1990-18418 19900823
DT Utility
FS Granted
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Cushman Darby & Cushman Intellectual Property Group of Pillsbury Madison & Sutro, LLP
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 17 Drawing Page(s)
LN.CNT 5414
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a conjugate of a solution stable G-CSF derivative and a water soluble polymer which is an acid stable physiologically active substance derived from naturally occurring G-CSF.

L2 ANSWER 27 OF 42 USPATFULL on STN
AN 96:103981 USPATFULL
TI Conjugates of vitamin B12 and proteins
IN Habberfield, Alan D., Pacific Palisades, CA, United States
Kinstler, Olaf B., Thousand Oaks, CA, United States
Pitt, Colin G., Thousand Oaks, CA, United States
PA Amgen Inc., Thousand Oaks, CA, United States (U.S. corporation)
PI US 5574018 19961112
AI US 1994-282384 19940729 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Achutamurthy, Ponnathapura
LREP Mazza, Richard J.
CLMN Number of Claims: 24
ECL Exemplary Claim: 1,2
DRWN 14 Drawing Figure(s); 13 Drawing Page(s)
LN.CNT 1385
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Therapeutically useful proteins are conjugated to vitamin B.sub.12 by covalent binding at the primary hydroxyl site of the ribose moiety. The resulting conjugates are biologically active and can be formulated into pharmaceutical compositions suitable for delivery by various routes of administration, preferably oral. Uptake in the gut following oral delivery is further enhanced by the co-administration of purified intrinsic factor.

L2 ANSWER 28 OF 42 USPATFULL on STN
AN 94:51228 USPATFULL

TI Continuous release pharmaceutical compositions
 IN Camble, Roger, Macclesfield, England
 Timms, David, Macclesfield, England
 Wilkinson, Anthony J., Macclesfield, England
 PA Imperial Chemical Industries PLC, London, England (non-U.S. corporation)
 PI US 5320840 19940614
 AI US 1991-734225 19910722 (7)
 PRAI GB 1990-16138 19900723
 GB 1990-18414 19900823
 GB 1990-18415 19900823
 GB 1990-18416 19900823
 GB 1990-18417 19900823
 GB 1990-18418 19900823
 DT Utility
 FS Granted
 EXNAM Primary Examiner: Russel, Jeffrey E.
 LREP Cushman, Darby & Cushman
 CLMN Number of Claims: 10
 ECL Exemplary Claim: 1
 DRWN 19 Drawing Figure(s); 17 Drawing Page(s)
 LN.CNT 5305

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Pharmaceutical compositions for continuous release of a physiologically active substance in which the physiologically active substance comprises a polypeptide covalently conjugated to a water soluble polymer show particularly desirable release characteristics. Polypeptides for use in the pharmaceutical compositions include G-CSF and solution stable derivatives thereof, human calcitonin and interleukin-2. The material of the composition may be a polylactide or biodegradable hydrogel derived from an amphipathic block copolymer.

The compositions enable a therapeutically effective polypeptide to be continuously released over a prolonged period of time following a single administration of the pharmaceutical composition to a patient.

L2 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:706922 CAPLUS
 DN 139:219365
 TI Drug absorption-improving compositions containing .alpha.-tocopheryl polyethylene glycol succinate and glyceride/macrogol ester mixtures
 IN Takada, Kanji
 PA Japan
 SO Jpn. Kokai Tokkyo Koho, 5 pp.
 CODEN: JKXXAF
 DT Patent
 LA Japanese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2003252750	A2	20030910	JP 2002-50475	20020226
PRAI	JP 2002-50475		20020226		

AB The invention relates to a pharmaceutical compn. for promoting intestinal absorption and bioavailability of a water-sol. drug with poor- or low-absorbability, e.g. specified antibiotic and peptide, etc., wherein the compn. is characterized by contg. .alpha.-tocopheryl polyethylene glycol succinate (Eastman vitamin E TPGS NF) and an ester mixt. consisting of C6-18fatty acid glycerol ester and C6-18 fatty acid macrogol ester. A soln. contg. gentamicin sulfate, caprylocaproyl macrogol glyceride (Labrasol), and .alpha.-tocopheryl polyethylene glycol succinate was formulated for examine the bioavailability of gentamicin in rats.

L2 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:492424 CAPLUS
 DN 139:74025

TI G-CSF conjugates for therapeutic uses
 IN Nissen, Torben Lauesgaard; Andersen, Kim Vilbour; Hansen, Christian
 Karsten; Mikkelsen, Jan Moller; Schambye, Hans Thalsgaard
 PA Maxygen Holdings Ltd., USA
 SO U.S. Pat. Appl. Publ., 54 pp., Cont.-in-part of U.S. Ser. No. 904,196.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003118612	A1	20030626	US 2002-192294	20020710
	US 2002004483	A1	20020110	US 2001-760008	20010110
	US 6646110	B2	20031111		
	US 2003064922	A1	20030403	US 2001-904196	20010711
	US 6555660	B2	20030429		
	ZA 2002004623	A	20021211	ZA 2002-4623	20020610
	ZA 2002004625	A	20021211	ZA 2002-4625	20020610
PRAI	DK 2000-24	A	20000110		
	US 2000-176376P	P	20000114		
	DK 2000-341	A	20000302		
	US 2000-189506P	P	20000315		
	DK 2000-943	A	20000616		
	US 2000-215644P	P	20000630		
	US 2001-760008	A2	20010110		
	US 2001-904196	A2	20010711		
	DK 2002-447	A	20020322		
	DK 2002-708	A	20020508		

AB Polypeptide conjugates with G-CSF activity comprising a polypeptide having at least one introduced lysine residue and at least one removed lysine residue compared to the sequence of human G-CSF, and which are conjugated to 2-6 polyethylene glycol moieties are described. The conjugates have a low (in vitro bioactivity), a long in vivo half-life, a reduced receptor-mediated clearance, and provide a more rapid stimulation of prodn. of white blood cells and neutrophils than non-conjugated recombinant human G-CSF.

L2 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:360257 CAPLUS
 DN 138:336419
 TI Preparation of **polyethylene glycol**-coupled G
 -CSF for induction of granulopoiesis
 IN Zhao, Jian; Jin, Beiwen; Chen, Hu
 PA Peop. Rep. China
 SO Faming Zhuanli Shenqing Gongkai Shuomingshu, 16 pp.
 CODEN: CNXXEV
 DT Patent
 LA Chinese
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CN 1355252	A	20020626	CN 2000-127510	20001123
PRAI	CN 2000-127510		20001123		
AB	The invention relates to prepn. of a heterogeneous product of granulocyte colony-stimulating factor or G-CSF, a mixt. of G-CSF or its analog and polyethylene glycol (mol. wt. of 4,000-50,000 Da)-modified G-CSF (at a ratio of 15- 85:15:85), by coupling G-CSF with polyethylene glycol at 4-25.degree. and pH 8.0 for 5-40 h and removing the excess polyethylene glycol. The invention also relates to the medicinal compn. of the heterogeneous product.				

L2 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:261006 CAPLUS

DN 138:292712
 TI Polymer-bonded human granulocyte colony-stimulating factor (G-CSF) conjugates and use for treating hematopoietic disorders
 IN Nissen, Torben Lauesgaard; Andersen, Kim Vilbour; Hansen, Christian Karsten; Mikkelsen, Jan Moller; Schambye, Hans Thalsgaard
 PA Den.
 SO U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 760,008.
 CODEN: USXXCO
 DT Patent
 LA English
 FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003064922	A1	20030403	US 2001-904196	20010711
	US 6555660	B2	20030429		
	US 2002004483	A1	20020110	US 2001-760008	20010110
	US 6646110	B2	20031111		
	ZA 2002004623	A	20021211	ZA 2002-4623	20020610
	ZA 2002004625	A	20021211	ZA 2002-4625	20020610
	WO 2003006501	A2	20030123	WO 2002-DK482	20020710
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003118612	A1	20030626	US 2002-192294	20020710
	US 2003158375	A1	20030821	US 2002-318966	20021213
PRAI	DK 2000-24	A	20000110		
	US 2000-176376P	P	20000114		
	DK 2000-341	A	20000302		
	US 2000-189506P	P	20000315		
	DK 2000-943	A	20000616		
	US 2000-215644P	P	20000630		
	US 2001-760008	A2	20010110		
	US 2001-904196	A	20010711		
	DK 2002-447	A	20020322		
	DK 2002-708	A	20020508		

AB The invention relates to polypeptide conjugates comprising a polypeptide exhibiting G-CSF activity and having an amino acid sequence that differs from the amino acid sequence of human G-CSF in at least one specified introduced and/or removed amino acid residue comprising an attachment group for a non-polypeptide moiety, and having at least one non-polypeptide moiety attached to an attachment group of the polypeptide. The attachment group may e.g. be a lysine, cysteine, aspartic acid or glutamic acid residue or a glycosylation site, and the non-polypeptide moiety may e.g. be a polymer such as polyethylene glycol or an oligosaccharide. The conjugate, which has a reduced in vitro bioactivity compared to hG-CSF, has one or more improved properties such as increased biol. half-life and increased stimulation of neutrophils.

L2 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2003:247890 CAPLUS
 DN 138:396326
 TI Parsing the effects of binding, signaling, and trafficking on the mitogenic potencies of granulocyte colony-stimulating factor analogues
 AU Sarkar, Casim A.; Lowenhaupt, Ky; Wang, Peggy J.; Horan, Thomas; Lauffenburger, Douglas A.
 CS Department of Chemical Engineering Biotechnology Process Engineering

Center Department of Biology and Biological Engineering Division,
Massachusetts Institute of Technology, Cambridge, MA, 02139-4307, USA
SO Biotechnology Progress (2003), 19(3), 955-964
CODEN: BIPRET; ISSN: 8756-7938

PB American Chemical Society

DT Journal

LA English

AB The pharmacodynamic potency of a therapeutic cytokine interacting with a cell-surface receptor can be attributed primarily to three central properties: [1] cytokine/receptor binding affinity, [2] cytokine/receptor endocytic trafficking dynamics, and [3] cytokine/receptor signaling. Thus, engineering novel or second-generation cytokines requires an understanding of the contribution of each of these to the overall cell response. The authors describe here an efficient method toward this goal in demonstrated application to the clin. important cytokine granulocyte colony-stimulating factor (G-CSF) with a chem. analog and a no. of genetic mutants. Using a combination of simple receptor-binding and dose-response proliferation assays the authors construct an appropriately scaled plot of relative mitogenic potency vs. ligand concn. normalized by binding affinity. Anal. of binding and proliferation data in this manner conveniently indicates which of the cytokine properties-binding, trafficking, and/or signaling-are contributing substantially to altered potency effects. For the G-CSF analogs studied here, two point mutations as well as a poly(ethylene glycol) chem. conjugate were found to have increased potencies despite comparable or slightly lower affinities, and trafficking was predicted to be the responsible mechanism. A third point mutant exhibiting comparable binding affinity but reduced potency was predicted to have largely unchanged trafficking properties. Surprisingly, another mutant possessing an order-of-magnitude weaker binding affinity displayed enhanced potency, and increased ligand half-life was predicted to be responsible for this net beneficial effect. Each of these predictions was successfully demonstrated by subsequent measurements of depletion of these five analogs from cell culture medium. Thus, for the G-CSF system the authors find that ligand trafficking dynamics can play a major role in regulating mitogenic potency. The authors' results demonstrate that cytokine analogs can exhibit pharmacodynamic behaviors across a diverse spectrum of "binding-potency space" and that the anal. through normalization can efficiently elucidate hypotheses for the underlying mechanisms for further dedicated testing. The authors have also extended the Black-Leff model of pharmacol. agonism to include trafficking effects along with binding and signaling, and this model provides a framework for parsing the effects of these factors on pharmacodynamic potency.

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN

AN 2003:58123 CAPLUS

DN 138:135837

TI Therapeutic G-CSF conjugates with PEG for increased half-life

IN Nissen, Torben Lauesgaard; Andersen, Kim Vilbourn; Hansen, Christian
Karsten; Mikkelsen, Jan Moller; Schambye, Hans Thalsgard

PA Maxygen Holdings Ltd., Cayman I.

SO PCT Int. Appl., 106 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006501	A2	20030123	WO 2002-DK482	20020710
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,			

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
 TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
 CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
 NE, SN, TD, TG

US 2003064922 A1 20030403 US 2001-904196 20010711
 US 6555660 B2 20030429
 PRAI US 2001-904196 A 20010711
 DK 2002-447 A 20020322
 DK 2002-708 A 20020508
 DK 2000-24 A 20000110
 US 2000-176376P P 20000114
 DK 2000-341 A 20000302
 US 2000-189506P P 20000315
 DK 2000-943 A 20000616
 US 2000-215644P P 20000630
 US 2001-760008 A2 20010110
 AB Polypeptide conjugates with G-CSF activity comprising a polypeptide having
 at least one introduced lysine residue and at least one removed lysine
 residue compared to the sequence of human G-CSF, and which are conjugated
 to 2-6 polyethylene glycol moieties. The conjugates have a low in vitro
 bioactivity, a long in vivo half-life, a reduced receptor-mediated
 clearance, and provide a more rapid stimulation of prodn. of white blood
 cells and neutrophils than non-conjugates recombinant human G-CSF.
 L2 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2002:47154 CAPLUS
 DN 136:277611
 TI Pegylated cytokines. Potential application in immunotherapy of cancer
 AU Eliason, James F.
 CS Barbara Ann Karmanos Cancer Institute, Wayne State University, Detroit,
 MI, USA
 SO BioDrugs (2001), 15(11), 705-711
 CODEN: BIDRF4; ISSN: 1173-8804
 PB Adis International Ltd.
 DT Journal; General Review
 LA English
 AB A review. Conjugation of the polymer polyethylene glycol (PEG) to
 proteins can significantly decrease their clearance from plasma, thus
 increasing their half-lives in vivo. The increased half-life of
 PEG-proteins is directly proportional to the total mol. wt. of the
 construct. This approach has been used to design cytokine constructs that
 can be administered once a week, rather than on a daily or alternate-day
 schedule. Two cytokines for which this approach appears to be successful
 are PEG-interferon-.alpha.-2a (PEG-IFN.alpha.-2a) and PEG-granulocyte
 colony-stimulating factor (PEG-G-CSF). Both use high mol. wt. PEG (20 to
 40kD) to give sufficiently long duration in vivo. In the case of
 PEG-G-CSF conjugates, the in vivo efficacy is directly proportional to
 mol. wt., whereas the in vitro activity is inversely proportional,
 suggesting that overall duration of contact is more important than the
 affinity of the interaction. Conjugates of a no. of other cytokines have
 been prep'd., but until recently, few have used the high mol. wt. polymers.
 In the future, as this approach is taken to make new PEG-cytokine
 constructs, thorough pharmacokinetic studies will be essential for their
 development and clin. use.
 RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 2001:526095 CAPLUS
 DN 135:127157

TI Granulocyte colony-stimulating factor (G-CSF) conjugates for therapeutic uses

IN Nissen, Torben Lauesgaard; Andersen, Kim Vilbour; Hansen, Christian Karsten; Mikkelsen, Jan Moller; Schambye, Hans Thalsgaard

PA Maxygen Aps, Den.

SO PCT Int. Appl., 94 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001051510	A2	20010719	WO 2001-DK11	20010109
	WO 2001051510	A3	20020321		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP	1250154	A2	20021023	EP 2001-900105	20010109
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
BR	2001007561	A	20021119	BR 2001-7561	20010109
JP	2003519478	T2	20030624	JP 2001-551094	20010109
NZ	520261	A	20031031	NZ 2001-520261	20010109
ZA	2002004623	A	20021211	ZA 2002-4623	20020610
ZA	2002004625	A	20021211	ZA 2002-4625	20020610
NO	2002003315	A	20020905	NO 2002-3315	20020709
PRAI	DK 2000-24	A	20000110		
	DK 2000-341	A	20000302		
	DK 2000-943	A	20000616		
	WO 2001-DK11	W	20010109		
AB	The invention relates to polypeptide conjugates comprising a polypeptide exhibiting G-CSF activity and having an amino acid sequence that differs from the amino acid sequence of human G-CSF in at least one specified introduced and/or removed amino acid residue comprising an attachment group for a non-polypeptide moiety, and having at least one non-polypeptide moiety attached to an attachment group of the polypeptide. The attachment group may e.g. be a lysine, cysteine, aspartic acid or glutamic acid residue or a glycosylation site, and the non-polypeptide moiety may e.g. be a polymer such as polyethylene glycol or an oligosaccharide. The conjugate has one or more improved properties such as increased biol. half-life and reduced side effects.				
L2	ANSWER 37 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN				
AN	2000:380760 CAPLUS				
DN	133:115501				
TI	A single injection of polyethylene-glycol granulocyte colony-stimulating factor strongly prolongs survival of mice with systemic candidiasis				
AU	van Spriël, Annemiek B.; van den Herik-Oudijk, Ingrid E.; van de Winkel, Jan G. J.				
CS	Department of Immunology, University Medical Center, Utrecht, Neth.				
SO	Cytokine (2000), 12(6), 666-670				
	CODEN: CYTIE9; ISSN: 1043-4666				
PB	Academic Press				
DT	Journal				
LA	English				
AB	Systemic candidiasis is a life-threatening disease occurring in immunocompromised patients. Granulocyte colony-stimulating factor (G-CSF) reduces mortality in exptl. invasive candidiasis. Covalent conjugation of				

polyethylene-glycol (peg) to proteins increases their stability and in vivo bioactivity. In this study, the effect of a single s.c. injection of peg-G-CSF on lethal candidiasis was assessed. This was performed in acute and chronic candidiasis models in non-neutropenic FVB/N mice. Peg-G-CSF rapidly increased circulating polymorphonuclear leukocyte (PMNL) nos. in mice, sustaining high for >4 days. Candida albicans outgrowth from kidneys of infected mice was strongly reduced after peg-G-CSF treatment (5.76 log cfu/g kidney vs. 7.66 control), with absence of hyphal outgrowth and enhanced PMNL influx. Moreover, peg-G-CSF increased survival of C. albicans-infected mice, whereas efficacy of uncoupled G-CSF was obtained only after repeated treatment. These data document a potent in vivo biol. effect of peg-G-CSF, resulting in strongly enhanced resistance against systemic candidiasis. (c) 2000 Academic Press.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1998:802004 CAPLUS
DN 130:165112
TI New PEG2 type polyethylene glycol derivatives for protein modification
AU Yamasaki, Motoo; Okabe, Masami; Suzawa, Toshiyuki; Yokoo, Yoshiharu
CS Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Tokyo, 194-8533, Japan
SO Biotechnology Techniques (1998), 12(10), 751-754
CODEN: BTECE6; ISSN: 0951-208X
PB Chapman & Hall
DT Journal
LA English
AB Although proteins with 2,4-bis (o-methoxypolyethylene glycol)-6-chloro-s-triazine (PEG2-Cl) as a divalent PEG modification have some advantages compared to proteins with the linear PEG modification, PEG2Cl cannot react with amino groups at neutral pH. Therefore, we have prepd. new PEG2 derivs. that have an activated ester as the functional group. We confirmed that these derivs. are useful for the divalent modification of proteins, such as bsOD and rhG-CSF.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1997:25409 CAPLUS
DN 126:84668
TI Pharmacokinetics and pharmacodynamics of a recombinant human granulocyte colony-stimulating factor
AU Kuwabara, Takashi; Kobayashi, Satoshi; Sugiyama, Yuichi
CS Pharmaceutical Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Shizuoka, 411, Japan
SO Drug Metabolism Reviews (1996), 28(4), 625-658
CODEN: DMTRAR; ISSN: 0360-2532
PB Dekker
DT Journal; General Review
LA English
AB A review, with 66 refs., of G-CSF which discusses: pharmacokinetics and pharmacodynamics in exptl. animals; pharmacokinetics and pharmacodynamics in humans; contribution of receptor-mediated endocytosis to G-CSF clearance; and pharmacokinetics and pharmacodynamics of polyethylene glycol modified G-CSF.

L2 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:401731 CAPLUS
DN 125:50109
TI Chemical modification of N-terminus of protein to improve stability for therapeutical uses
IN Kinstler, Olaf B.; Gabriel, Nancy E.; Farrar, Christine E.; Deprince, Randolph B.

PA Amgen Inc., USA
 SO PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9611953	A1	19960425	WO 1995-US1729	19950208
	W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, UZ				
	RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5824784	A	19981020	US 1994-321510	19941012
	CA 2178752	AA	19960425	CA 1995-2178752	19950208
	CA 2307142	AA	19960425	CA 1995-2307142	19950208
	AU 9518419	A1	19960506	AU 1995-18419	19950208
	AU 706700	B2	19990624		
	EP 733067	A1	19960925	EP 1995-910233	19950208
	EP 733067	B1	19990512		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	ZA 9501008	A	19961018	ZA 1995-1008	19950208
	CN 1139932	A	19970108	CN 1995-191454	19950208
	CN 1071760	B	20010926		
	JP 09506116	T2	19970617	JP 1995-513191	19950208
	EP 822199	A2	19980204	EP 1997-117514	19950208
	EP 822199	A3	20011024		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
	AT 179991	E	19990515	AT 1995-910233	19950208
	ES 2131811	T3	19990801	ES 1995-910233	19950208
	IL 112585	A1	20000831	IL 1995-112585	19950208
	JP 2003155299	A2	20030527	JP 2002-288746	19950208
	JP 2003327600	A2	20031119	JP 2003-106520	19950208
	US 5985265	A	19991116	US 1997-879760	19970620
	HK 1008826	A1	20000331	HK 1998-109573	19980731
	AU 9948870	A1	19991111	AU 1999-48870	19990922
	AU 741659	B2	20011206		
	CN 1313343	A	20010919	CN 2000-130974	20001120
	US 2003053982	A1	20030320	US 2002-131956	20020425
	US 2003096400	A1	20030522	US 2002-264846	20021004
PRAI	US 1994-321510	A	19941012		
	AU 1995-18419	A3	19950208		
	CA 1995-2178752	A3	19950208		
	EP 1995-910233	A3	19950208		
	JP 1999-76959	A3	19950208		
	WO 1995-US1729	W	19950208		
	US 1997-879760	A3	19970620		
	US 1999-408113	B1	19990929		
	US 2001-817725	A1	20010326		
	US 2002-131956	A1	20020425		
AB	A method to enhance the in vivo stability of a protein such as G-CSF by chem. modification of its N-terminus is described. Methods and compns. relating to the attachment of water sol. polymers to G-CSF are provided. Also provided is chem. modified consensus interferon. A pharmaceutical compn. contg. the modified G-CSF or interferon is claimed. A method of prepg. a substantially homogeneous population of monopegylated G-CSF using reductive alkylation was demonstrated.				

L2 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1996:398572 CAPLUS
 DN 125:95821

TI Engineering G-CSF for improved depot formulation
 AU Camble, Roger
 CS ZENECA Pharmaceuticals, Macclesfield/Cheshire, SK10 4TG, UK
 SO Perspectives on Protein Engineering & Complementary Technologies,
 Collected Papers, International Symposium, 3rd, Oxford, Sept. 13-17, 1994
 (1995), Meeting Date 1994, 193-196. Editor(s): Geisow, Michael J.; Epton,
 Roger. Publisher: Mayflower Worldwide, Kingswinford, UK.
 CODEN: 622QAP

DT Conference

LA English

AB The objective was to identify a G-CSF deriv. compatible with continuous
 release from polylactide-co-glycolide copolymers similar to those used for
 the Zoladex depot. Substitutions designed to increase surface
 hydrophilicity or conformational stability were made in the amino acid
 sequence and highly potent analogs identified with improved soln.
 stability at high protein concn. Chem. modification of analogs by
 reaction with a large excess of activated monomethyl **polyethylene**
glycol provided **G-CSF** derivs. with the desired
 profile of release from depot formulations.

L2 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1993:473127 CAPLUS

DN 119:73127

TI Preparation of chemically modified granulocyte-colony stimulating factor
 (G-CSF) derivatives

IN Ishikawa, Masatoshi; Okada, Yuji; Matsuki, Shigeru

PA Kirin-Amgen, Inc., Japan

SO Jpn. Kokai Tokkyo Koho, 13 pp.

CODEN: JKXXAF

DT Patent

LA Japanese

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 04164098	A2	19920609	JP 1990-418953	19901214
PRAI	JP 1990-56291		19900307		

AB The title G-CSF derivs. H-(Met)n-Thr-Pro-Leu-Gly-Pro-Ala-Ser-Ser-Leu-Pro-
 Gln-Ser-Phe-Leu-Leu-Lys-X-Leu-Glu-Gln-Val-Arg-Lys-Ile-Gln-Gly-Asp-Gly-Ala-
 Ala-Leu-Gln-Glu-Lys-Leu-Cys-Ala-Thr-Tyr-Lys-Leu-Cys-His-Pro-Glu-Glu-Leu-
 Val-Leu-Leu-Gly-His-Ser-Leu-Gly-Ile-Pro-Trp-Ala-Pro-Leu-Ser-Ser-Cys-Pro-
 Ser-Gln-Ala-Leu-Gln-Leu-Ala-Gly-Cys-Leu-Ser-Gln-Leu-His-Ser-Gly-Leu-Phe-
 Leu-Tyr-Gln-Gly-Leu-Leu-Gln-Ala-Leu-Glu-Gly-Ile-Ser-Pro-Glu-Leu-Gly-Pro-
 Thr-Leu-Asp-Thr-Leu-Gln-Leu-Asp-Val-Ala-Asp-Phe-Ala-Thr-Thr-Ile-Trp-Gln-
 Gln-Met-Glu-Glu-Leu-Gly-Met-Ala-Pro-Ala-Leu-Gln-Pro-Thr-Gln-Gly-Ala-Met-
 Pro-Ala-Phe-Ala-Ser-Ala-Phe-Gln-Arg-Arg-Ala-Gly-Gly-Val-Leu-Val-Ala-Ser-
 His-Leu-Gln-Ser-Phe-Leu-Glu-Val-Ser-Tyr-Arg-Val-Leu-Arg-His-Leu-Ala-Gln-
 Pro-OH (I; X = any amino acid except Cys; n = 0, 1) consists of G-CSF
 polypeptides, which is an expression product of an exogenous DNA by a host
 cell, bonded to a polyethylene glycol, particularly through the NH2 group
 of I. The G-CSF derivs. have prolonged serum retention time,
 pharmaceutical activity, and improved thermal stability and yield. Thus,
 human I (X = Ala, n = 0) and methoxypoly(ethylene glycol) succinimidyl
 succinate (M.W. .apprx.4,500) (II) (40 equiv. based on the free NH2 groups
 in I) were reacted in 0.25 Na borate buffer at 4.degree. for 1 h and,
 after exchanging the buffer soln. by using Sephadex G25 previously
 equilibrated with 10 mM NH4HCO3, was purified by DEAE ion exchange
 chromatog. to give a poly(ethylene glycol)-modified human G-CSF-Ala17.
 This at 10 .mu.g/kg i.v. increased the serum leukocyte counts in mice from
 9.4, 11.7, and 11.7 (control) to 25.6, 18.0, and 15.1 after 24, 48, and 72
 h, resp. vs. 22.3, 11.3, and 9.7, resp. for the unmodified G-CSF.

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FILE CONTAINS CURRENT INFORMATION.
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